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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,541	04/26/2002	Larry A. Wheeler	17400(BAR)	1687

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,541	WHEELER ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005 and 20 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,18-22 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,18-22 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/20/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communications filed on 6/13/2005 and 6/20/2005. The amendment filed 6/13/2005 is acknowledged. The amendment has been entered. Claims 16, 18-22 and 30 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/20/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is indefinite because it depends on any of claims 16-22. However, claim 17 has been cancelled. As such, claim 30 depends on a rejected claim (i.e. claim 17), thus rendering

claim 30 indefinite. It is noted that amending claim 30 such that it is not dependent on claim 17 would obviate this rejection. In the interest of compact prosecution, claim 30 will be interpreted as depending on any one of claims 16, 18-22.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 6/20/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16, 18-22 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application publication No US 2002/0040015 A1 (Miller at al.) in view of Wheeler et al. (Europ. Jour. Ophthal., JAN-MAR 1999).

Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound and a neuroprotectant compound that represses apoptosis in cells or tissues surrounding the treatment (e.g., see abstract; paragraph 18; claims

20-31, etc.). It is noted the specification of the instant application acknowledges that PDT (which is recognized as requiring the use of a photosensitizing agent) can damage optical neural tissue. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). Regarding the anti-apoptotic compound, Miller teaches that the anti-apoptotic compound is useful for decrease a cell's sensitivity to PDT, and specifically indicates that BDNF, PEDF are two anti-apoptotic compounds that can be used in the method (it is noted that the instant specification also discloses BDNF and PEDF as neuroprotective compounds).

Miller does not teach that the neuroprotectant compound is Brimonidine.

However, Wheeler teaches that Brimonidine is an alpha-2 agonist compound that is neuroprotective in animal models of retinal and optic nerve injury (e.g., see title, abstract, etc.).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to perform the method taught by Miller and substitute Brimonidine as the neuroprotective agent with a reasonable expectation of success because Wheeler teaches that Brimonidine is a neuroprotective agent.

One of ordinary skill in the art would have been motivated to substitute Brimonidine as the neuroprotective agent in Miller's method because Wheeler teaches that Brimonidine is an anti-apoptotic neuroprotective agent that can be used to protect target cells from neuronal injury (e.g., see page S20-S21, etc.). Therefore, the anti-apoptotic compounds used in the method taught by Miller and Brimonidine are art recognized equivalents (see MPEP 2144.06-2144.07 regarding substitution of equivalents).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16, 18-22 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,856,329 (hereafter '329) in view of Miller et al (US 2002/0040015 A1).

The '329 patent teaches that Brimonidine is neuroprotective agent that can be used to protect an optic nerve from damage caused by a noxious action, (e.g., see claims, especially claims 1 and 12).

The '329 patent does not teach that the noxious action is photodynamic therapy.

However, as indicated above, Miller teaches a method and composition for treating conditions of the eye. Specifically, Miller teaches a method for photodynamic therapy (PDT) of ocular conditions characterized by the presence of unwanted choroidal neovasculature which includes enhancing the PDT method by administering an antiangiogenic compound and a neuroprotectant compound that represses apoptosis in cells or tissues surrounding the treatment (e.g., see abstract; paragraph 18; claims 20-31, etc.). It is noted the specification of the instant

application acknowledges that PDT (which is recognized as requiring the use of a photosensitizing agent) can damage optical neural tissue. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). Regarding the anti-apoptotic compound, Miller teaches that the anti-apoptotic compound is useful for decrease a cell's sensitivity to PDT, and specifically indicates that BDNF, PEDF are two anti-apoptotic compounds that can be used in the method (it is noted that the instant specification also discloses BDNF and PEDF as neuroprotective compounds).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to use the method taught by the '329 patent (using Brominidine as a neuroprotectant) to protect ocular tissue from the noxious effects of PDT, with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to use the method to protect ocular tissue from PDTR damage because the '329 patent is disclosed as a method of protecting ocular tissue from damage caused by a any noxious agent and the prior art recognizes that PDT can cause damage to ocular tissue.

Response to Arguments

Applicant's arguments filed 6/13/2005 have been fully considered.

With respect to the rejection of claims 16, 18 and 30 under 35 USC 112, second paragraph, Applicant's arguments, in view of the amendment, are persuasive. Therefore the rejection has been withdrawn. However, claim 30 is now under 35 USC 112, 2nd paragraph in view of the amendment filed 6/13/2005 for the reasons indicated herein.

With respect to the rejection of claims under 35 USC 112, first paragraph, Applicant's arguments, in view of the amendment, are persuasive. Therefore the rejection has been withdrawn.

With respect to the rejection of claims under 35 USC 122, Applicant's arguments, in view of the amendment, are persuasive. Therefore the rejection has been withdrawn.

With respect to the objection to the specification and claims, Applicant's arguments, in view of the amendment, are persuasive. Therefore the objection(s) has been withdrawn.

With respect to the rejection of claims under 35 USC 103, Applicant's arguments filed 6/13/2005 have been fully considered but they are not persuasive. Applicants argue there is no motivation to combine the teachings of Wheeler and Miller. Applicants also argue that the combination of Wheeler and Miller fails to disclose, teach or suggest all of the elements of the present claims. Specifically, Applicants argue that Miller teaches using peptide inhibitors of apoptosis, not small molecule chemical compound inhibitors of apoptosis. As such, Applicants contend that one of ordinary skill would not have been motivated to use small chemical compound inhibitors of apoptosis, such as brimonidine. Applicants also argue that Wheeler does not teach using brimonidine to protect ocular neural tissue from photodynamic therapy (PDT) injury. Applicants also assert that Miller does not disclose, teach or suggest the use of

brimonidine and Wheeler does not disclose, teach or suggest the amounts of brimonidine recited in the claims.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Miller teaches the general concept of using PDT and antiangiogenic factors in combination for treating choroidal neovascularization in an affected eye. Miller also teaches the use of an apoptosis inhibitors to protect the surrounding tissue (e.g., the optic nerve) from the effects (e.g., atrophy) caused by the treatment. Although Miller does not explicitly teach the use of brimonidine as the apoptotic inhibitor, brimonidine was recognized in the art as an apoptosis inhibitor (e.g., see Wheeler). Therefore, the apoptotic inhibitors taught by Miller and Wheeler are art recognized equivalents. It is prima facie obvious to substitute one art recognized equivalent for another (e.g., see MPEP 2144.06-2144.07). Applicants are reminded that MPEP 2144.06 states that an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious (In re Fout, 675 F.2d 297, 213 USPQ

532 (CCPA 1982)). Furthermore, since brimonidine was recognized in the art as effective inhibitor of ocular neural cell death, the exact amount of brimonidine to use to protect cells from cell death would be a matter of routine optimization (see MPEP 2144.05 - II Optimization of Ranges). Applicants are reminded that MPEP 2144.05 indicates:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); and,
>
> A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

In the instant case, the art recognizes that brimonidine is a which achieves inhibition of ocular neural cell apoptosis induced by PDT. Therefore, the determination of the optimum or workable ranges of brimonidine can be characterized as routine experimentation.

With respect to obvious-type double patenting rejection, Applicants argue that the '329 patent does not disclose, teach or suggest a method of protecting ocular neural tissue from damage caused by PTD treatment. Applicants assert that the claims of the '329 patent are broadly directed to protecting nerve cells in a mammal suffering noxious action or at risk of suffering noxious actions.

In response, the '329 patent teaches that Brimonidine is neuroprotective agent that can be used to protect an optic nerve from damage caused by a noxious action, (e.g., see claims, especially claims 1 and 12). The '329 patent does not specifically teach that the noxious action is photodynamic therapy. However, PDT was recognized in the prior art as a noxious action that

caused optic nerve damage when used to treat choroidal neovascularization (e.g., see Miller, paragraphs [0006]-[0009]). Furthermore, the instant specification acknowledges that PDT was recognized in the prior art as a noxious action that caused optic nerve damage. Specifically, the instant application teaches that PDT incorporating high doses of the photosensitizing agent vertporfin, "[R]esult in long term or permanent scarring of the retina, chronic absence of photoreceptor cells, and **optic nerve atrophy**." (Emphasis added; see p. 3, first full paragraph). As such, the '329 patent teaches a method of treating a broad genus of "noxious actions" using brimonidine, and PDT was known in the art as a noxious action. Therefore, it would have been obvious to use the method taught by the '329 patent to treat the noxious action that is PDT (as taught by Miller).

Therefore, Applicants' arguments are not persuasive.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Anne-Marie Falk
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PRIMARY EXAMINER